

Rapid Review of the literature: Assessing the infection prevention and control measures for the prevention and management of COVID-19 in health and care settings

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Contents

1. Aim	4
2. Objectives	4
3. Search Strategy	4
Evidence updates	5
Results.....	5
1. Epidemiology	6
2. Personal protective equipment.....	17
3. Hand hygiene.....	23
4. Survival in the environment.....	24
5. Environmental decontamination	25
6. Areas for further research	27
References	28

Abbreviations

ABHR	Alcohol based hand rub
AGP	Aerosol-generating procedure
FFP2	Filtering face piece respirator (class 2)
FFP3	Filtering face piece respirator (class 3)
FRSM	Fluid-resistant surgical face mask
HDU	High dependency unit
HPS	Health Protection Scotland
ICU	Intensive care unit
ITU	Intensive therapy unit
MERS-CoV	Middle East respiratory syndrome coronavirus
NIPCM	National Infection Prevention and Control Manual
NERVTAG	New and Emerging Respiratory Virus Threat Assessment Group
PPE	Personal protective equipment
RPE	Respiratory protective equipment
SARS-CoV	Severe acute respiratory syndrome coronavirus
SARS-CoV-2	Severe acute respiratory syndrome coronavirus 2
WHO	World Health Organization

1. Aim

To provide a rapid review of the scientific evidence base to inform the infection prevention and control measures required for the prevention and management of COVID-19 in health and care settings.

2. Objectives

Objectives for the rapid review were to establish the following:

- The epidemiology of COVID-19;
- The personal protective equipment (PPE) requirements;
- The requirements for hand hygiene;
- The environmental survivability of COVID-19;
- The requirements for cleaning/decontamination of the care environment.

3. Search Strategy

Academic databases were searched on 5th March 2020 to identify relevant literature and additional hand searching was conducted. As this was a rapid review, evidence was critiqued but not formally graded with the use of an appraisal tool.

The search terms were as follows:

1. COVID-19.mp.
2. SARS-CoV-2.mp.
3. 2019-nCoV.mp.
4. novel coronavirus.mp.
5. exp coronavirus/
6. 1 or 2 or 3 or 4 or 5
7. exp infection control/
8. exp disinfection/

9. exp decontamination/
10. exp personal protective equipment/
11. surgical mask?.mp.
12. surgical mask?.mp.
13. hand hygiene.mp.
14. clean*.mp.
15. transmission.mp.
16. 7 or 8 or 9 or 10 or 11 or 12 or 13 or 14 or 15
17. 6 and 16
18. limit 17 to English language
19. limit 18 to yr="2020 -Current"

Evidence updates

The emerging evidence base on COVID-19 is rapidly changing. To account for this, published literature will be screened on a weekly basis and monthly evidence tables produced. Updates to the rapid review will be made as emerging evidence arises and if the evidence base indicates that a change to recommendations is required.

Results

An overarching limitation of all identified evidence is the novel nature of SARS-CoV-2 and the limited ability for robust research at the early stages of an outbreak. Most papers highlight the need for further research.

1. Epidemiology

Transmission routes

The transmission of COVID-19 is thought to occur mainly through respiratory droplets generated by coughing and sneezing, and through contact with contaminated surfaces. Preliminary evidence indicates the routes of transmission to be droplet¹⁻¹⁰ and contact.^{1, 3, 6-11} Evidence also supports indirect contact.^{1, 6, 7, 9, 10} These transmission routes are supported by National¹²⁻¹⁴ and international guidance.^{15, 16}

Currently there is no clear evidence of airborne transmission of SARS-CoV-2. Tests have not been able to identify viable virus or viral replication in air samples collected from hospital inpatient rooms.¹⁹ Positive air samples from ICUs may be a reflection of the higher aerosol risk that is related to aerosol-generating procedures (AGPs) that are conducted in these high risk clinical settings.

Aerosol-generating procedures have been associated with an increased risk of transmission of previous coronaviruses (SARS-CoV and MERS-CoV)^{16, 20} and a number of AGPs (mostly airway management) have been implicated as risk factors for transmission of SARS-CoV-2 to health and care workers (HCWs)^{9, 21} however attributing risk to specific procedures with any level of certainty is challenging. The concept of an 'aerosol generating procedure' arose following the study of SARS-CoV transmission events where it was observed that a pathogen, which was consistently associated with droplet or contact transmission, appeared to have the potential to infect HCWs via the airborne route during specific procedures. This is reflected in the World Health Organisation's (WHO) definition of an AGP which states that they create the potential for airborne transmission of infections that may otherwise only be transmissible by the droplet route.²² It should also be recognised that as well as producing aerosols, these procedures produce larger droplet particles.²³⁻²⁵

The WHO further defines an AGP as those procedures which result in the production of airborne particles (aerosols).²² Particles which they describe as being <5 micrometres (µm) in size and as such can remain suspended in the air, travel over a distance and may cause infection if inhaled.²² These particles are created by air currents moving over the surface of a film of liquid, the faster the air, the smaller the particles produced.²² Using this definition there are potentially many medical or patient care procedures which could be classed as 'aerosol generating' but whether they lead to an increased risk of respiratory

infection transmission is a different and important question. The 2014 WHO guidance is specific in its wording, outlining that '*some procedures potentially capable of generating aerosols are associated with increased risk of SARS transmission to health-care workers*' and they outline that, regarding pandemic and epidemic prone acute respiratory infections, it is for these procedures that airborne precautions should be used.²² Medical and patient care procedures should be assessed based not only on their capacity to generate aerosols but also on their ability to generate infectious aerosols and an association with relevant transmission events. Health Protection Scotland conducted a review of the evidence base for a number of clinical procedures for their consideration as AGPs in relation to increased risk of respiratory infection transmission, in collaboration with the Department of Health and Social Care's New and Emerging Respiratory Virus Threat Assessment Group (NERVTAG).²⁶ There are no changes to the current AGP list however additional clarity was provided regarding dental procedures and surgical/post-mortem procedures; risk during dentistry is related to the use of high speed devices such as ultrasonic scalers and high speed drills. In surgery/post-mortem, risk is related to the use of high speed cutting if this involves the respiratory tract or paranasal tissues.

Clinical presentation

Whilst it is apparent that there is variation in the severity and range of symptoms experienced, the most frequently reported symptoms include fever and cough.²⁷⁻³⁴ Initial UK data also reflects this.³⁵ In China, data indicates that pneumonia was the most frequently reported symptom.²⁷ Paediatric cases tend to have less severe disease, are hospitalised less frequently than adult patients and are less likely to be admitted to ICU.³⁶⁻⁴⁰

It is widely recognised that those individuals with underlying comorbidities (diabetes, cardiovascular disease, lung disease) have an increased risk of ICU admission and mortality.^{41, 42} Data from a UK cohort has shown that cardiovascular and cerebrovascular disease was significantly more common in patients that had died by 14 days (90% vs 48% in those still alive) and of these congestive cardiac failure was the most notably associated with non-survival (35% vs 11%).³⁵ Median age in this study was 75 years. Case fatality was 21%; the authors state this was much higher than that reported by other studies of all hospitalised patients; the age of the cohort was also higher. This was also the case at a South West London hospital in which case fatality was 32.6% in a 500 patient cohort; average age was 69 years (SD 19.23, range 1 week to 88 years).⁴³ It is widely recognised

that older age groups have higher rates of underlying comorbidities and both have a correlation with a higher risk of COVID-19 mortality.

Analysis of 53,000 confirmed cases found that 7.7% experienced gastrointestinal symptoms, with approximately 5.7% experiencing diarrhoea.⁴⁴ The incidence of diarrhoea is more variable in smaller studies (2-50%).^{29, 31, 34, 35, 39, 45-50} Initial reports from mainland China suggest that nausea and vomiting are also infrequently reported (5.0% of 1099 confirmed cases).⁵¹ A number of early papers cited the need for more research into the possibility of faecal-oral transmission^{2, 6, 7, 9-11, 52, 53} following the discovery of viral RNA in the stool samples of COVID-19 patients.^{40, 54-59} Early studies reported on single patient cases^{54, 55, 57, 60} and/or lacked robust clinical data^{54, 56} (i.e. time course of illness, incubation period) which limited interpretation of the epidemiological significance of clinical samples. Emerging evidence has shown that viral RNA can be detected in stool in both children and adults after clearance in respiratory samples⁴⁸ and following resolution of symptoms.^{58, 59, 61} It is possible that the presence of viral RNA in stool is due to clearance from the mouth/throat into the gastrointestinal tract from swallowing. The transmission risk from non-respiratory samples is still being investigated; initial attempts at live virus isolation from stool have been unsuccessful.⁶² Wolfel et al, in the absence of histopathology, analysed the presence of viral sgRNA in clinical samples, which is only transcribed in infected cells and therefore can indicate the presence of actively-infected cells.⁶² They reported 'no or only minimal' indication of replication in stool by this method however this was a small study (n=9) and an area of research that requires further work. Limited data from endoscopic examination of infected patients has revealed positive staining of viral host receptor ACE2 in gastrointestinal epithelial cells, leading to the suggestion that gastrointestinal cells are actively infected⁵⁹ however this is a single study and an area of research that requires further investigation. To date there is no evidence of direct human-to-human transmission from faecal material.

It is worth noting that the application of standard infection control precautions (SICPs) would prevent ongoing transmission via the faecal-oral route.

Viral RNA has also been detected in blood samples from infected patients.^{56, 63-65} However transmission risk via the blood would be expected to be very low and transmission via this route has not been previously reported for respiratory viruses.

Viral RNA has not been detected in vaginal fluid⁶⁶ or in semen or testicular biopsy samples in the small number of those tested.⁶⁷ Detection has been reported in urine in a small

number of cases.^{65, 68} Viral load in urine was low but detectable and cytopathic effects were observed 3 days after inoculation onto Vero E6 cells.⁶⁸ These findings do not indicate infection of the kidneys or bladder however there is a possibility of transmission via the urine.

SARS-CoV-2 has been detected in the tears and conjunctival secretions in a small number of COVID-19 patients with conjunctivitis^{4, 69-71} leading to the suggestion that transmission could be possible via the mucous membranes of the eyes.^{72, 73} All secretions (except sweat) and excretions from patients with known or suspected COVID-19, should therefore be regarded as potentially infectious.

There is limited evidence regarding mother-to-child transmission. The majority of small studies describe development of COVID-19 in the third trimester with subsequent caesarean deliveries.⁷⁴⁻⁷⁸ Five rapid systematic reviews found no clear evidence of vertical transmission.⁷⁹⁻⁸⁴ Only one neonate has tested positive by RT-PCT 24 hrs after caesarean birth with additional positive obstetric tissue sample (amniotic fluid).⁸⁵ Seven reports describe positive neonatal samples in 10 neonates within 36 hrs of birth but obstetric samples were either not collected⁸⁶⁻⁸⁸ or tested negative.^{75, 89-91} All neonates were delivered by caesarean section; the majority of mothers (8/10) had mild infection (1 severe, 1 unreported) and all were in the 3rd trimester. Antibody testing was conducted in one neonate born to a mother with severe infection and both neonatal IgM and IgG tests were negative.⁸⁷ The majority of studies which have tested obstetric samples have not been able to detect viral RNA in amniotic fluid, cord blood, placenta, or breast milk in those tested.^{79, 80, 84, 92-94} There have been no reports of transmission to neonates associated with vaginal birth.^{82, 93-96} One neonate delivered vaginally in Italy developed symptoms and tested positive 3 days after birth but it is not clear if the baby was isolated from the mother after birth.⁹⁷ Whilst many studies describe IPC and isolation measures put in place during and following birth, it is possible that COVID-19 may have been transmitted to neonates from routes other than vertical; immediate testing on delivery may provide more clarity. Overall, evidence suggests very low risk of vertical transmission.

Atypical presentations

Atypical presentations include cases that do not display the typical clinical symptoms (fever, cough) (which constituted the case definition to date) but may test positive or show radiographic abnormalities (i.e. ground-glass opacity). The absence of respiratory

symptoms/fever has been reported in children^{36, 63, 98-100} and adults^{30, 49, 101}, with diagnosis often relying on RT-PCR and radiological investigation. Conjunctivitis in the absence of any other symptoms has also been reported.^{71, 102} The risk of transmission from these individuals, and whether it differs from that of individuals with typical presentations, has not been determined.

An atypical presentation occurred in an Italian national evacuated from China and quarantined on arrival with 56 others as a precautionary measure.⁶⁰ This case was a healthy 28 year old male who had no respiratory symptoms but had mild conjunctivitis and slight tonsillar exudate in the presence of positive naso- and oro-pharyngeal samples and stool samples. No transmission events from this case were reported. Hormati et al provide a brief report on the admission of two patients to a gastroenterology clinic in Iran with unusual gastrointestinal symptoms; both tested positive for COVID-19 in the absence of respiratory symptoms or fever.¹⁰³ Again, no transmission events were reported from these patients. A case report describes possible transmission from a 94 year old patient with atypical presentation (delirium, abdominal pain).¹⁰⁴ Nine HCWs and another inpatient developed COVID-19 after the patient was treated in three wards over 5 days with no infection control precautions, highlighting that there is risk of transmission from atypical presentations where no precautions are taken. Based on the increasing number of reports of atypical presentation, it may be pragmatic to consider widening the case definition as more evidence arises.

Asymptomatic transmission

A study by Ma et al (*not peer-reviewed*) that assessed clinical symptoms reported by 7 countries, calculated that, among RT-PCR-positive cases with relevant information (n=329), 49 (15%) were asymptomatic however it was not stated if radiographic symptoms were present.²⁸ Smaller studies have also reported positive asymptomatic cases, identified during contact tracing, that remained asymptomatic up until the point of negative RT-PCR conversion.¹⁰⁵⁻¹⁰⁷ To date, there has been limited evidence of transmission from positive-asymptomatic cases. A number of studies report on identification of viral RNA in clinical samples in asymptomatic patients^{61, 63, 108-110} however only one of these studies provides evidence of possible transmission. Contact tracing identified a possible asymptomatic index case in a family cluster in China; this case had normal CT imaging and no symptoms.¹¹⁰ It would appear that asymptomatic cases appear to be younger. A growing number of paediatric cases have been reported detailing asymptomatic presentations with

positive clinical samples however transmission events from these cases could not be proven.^{37, 61, 63, 106, 108, 111} Such studies are limited by their small sample size and observational nature and often lack robust clinical data.

Pre-symptomatic transmission

Possible transmission in the incubation period has been reported in a number of studies. A recent report detailed possible pre-symptomatic transmission in 7 community case clusters in Singapore; date of exposure could be determined in 4 clusters which suggested transmission occurring 1-3 days prior to symptom onset from source patients.¹¹²

Rothe et al report a single case of a Chinese national that travelled to Germany for business and reported hearing coughing from the rows behind on the airplane but was asymptomatic for the duration of contact with German colleagues.¹⁰⁹ Having developed symptoms on return to China, contact tracing was carried out and two German colleagues were identified as positive with mild symptoms.

Contact during the incubation period during a conference was identified as a possible mode of transmission from a single person to 2 family clusters in China; symptoms in the index case developed 2 days after the conference.¹¹³ Transmission in a cluster of young people (16-23yr olds) in China was linked to an asymptomatic index case who had contact with all persons in the cluster; all cases including the index case subsequently developed symptoms.¹¹⁴ The estimated incubation period was notably short (median 2 days) in this study. Two further cases of pre-symptomatic transmission were implicated in familial clusters in China; both cases had contact with a pre-symptomatic individual from Wuhan.¹¹³ Gao et al also describe possible pre-symptomatic transmission in the incubation period in a cluster of community cases.¹¹⁵ As with the aforementioned studies, there were no severe or critical patients in this cohort.

It is notably that these studies did not have clinical data available in the incubation period and relied on contact tracing analysis. As clinical sampling may not be widely conducted on mild/community-based cases (or asymptomatic individuals), there may continue to be a paucity of data in relation to determination of asymptomatic/pre-symptomatic transmission. The majority of evidence to date continues to point towards transmission occurring predominantly during the symptomatic period.

Nosocomial transmission

Data regarding symptoms in HCWs is limited but suggests a mirroring of symptoms experienced by the community/general population. In a Dutch cohort of 86 COVID-19-positive HCWs, the majority suffered relatively mild disease and 93% met a case definition of fever and/or coughing and/or shortness of breath.¹¹⁶ Other symptoms included headache, runny nose, sore throat, chest pain, and diarrhoea. A large proportion (63%) of those screened worked whilst being symptomatic, therefore the possibility of HCW-HCW and HCW-patient transmission (or indeed community transmission) cannot be ruled out, especially considering only 3% reported exposure to a positive inpatient.

There are reports of nosocomial transmission during the earlier stages of the epidemic; a COVID-19 outbreak on the paediatric dialysis unit of a German hospital involved transmission from an index patient to 7 HCWs and 3 patients.¹¹⁷ Transmission from an undiagnosed neurosurgery patient to 12 HCWs occurred at a hospital in Wuhan; appropriate PPE was not worn, with many HCWs not wearing surgical masks.¹¹⁸ Reports from a South West London hospital revealed that 51 of 500 analysed admissions developed COVID-19 nosocomially while inpatients.⁴³ A case report describes possible transmission from a 94 year old patient with atypical presentation (delirium, abdominal pain) to 9 HCWs and another inpatient after the patient was treated in three wards over 5 days with no infection control precautions.¹⁰⁴ Research conducted in March/April with NHS England Trusts to inform the Scientific Advisory Group for Emergencies (SAGE) suggests that nosocomial transmission of COVID-19 is occurring, with 8.2% of cases being diagnosed 14 days post-admission (inter-quartile range 3.8% to 12.0%). It was reported that few Trusts are assessing the possible involvement of HCWs in transmissions.

As sustained community transmission has occurred as the pandemic has progressed, it has become more challenging to identify true nosocomial transmission events. Screening of 1654 symptomatic HCWs by an English NHS Trust between March 10-31st identified 240 (14%) positive individuals; comparison of rates between staff in patient-facing and non-patient facing roles found no evidence of a difference, suggesting that data may reflect wider patterns of community transmission rather than nosocomial-only transmission.¹¹⁹ Mirroring of community transmission was also identified at a large public hospital in Madrid,¹²⁰ and at three hospitals in the Netherlands; contacts with COVID-19 individuals was reported from out-with the hospital and from contact with colleagues.¹²¹

Complete genome sequencing of 50 HCW and 18 patients suggested that the observed patterns were most consistent with multiple introductions into the hospital.¹²¹

It is notable that not all unprotected exposures to COVID-19 inpatients result in transmission; none of the 21 HCWs that reported contact with an undiagnosed patient with mild respiratory symptoms at a Swiss hospital tested positive when tested 7 days later.¹²² The patient underwent routine clinical examinations, blood draws, electrocardiograms, chest X-rays and had nasopharyngeal swabs taken; masks were never worn by HCWs during the patient's care.

Conclusion:

- Standard Infection Control Precautions (SICPs) should always be applied regardless of the infectious nature of the patient.
- Droplet precautions should be implemented when in close contact (within 2 metres), or providing direct patient care to a suspected/confirmed COVID-19 patient.
- Airborne precautions should be implemented when undertaking an AGP.

Incubation period

Many of the studies published to date are limited by small sample sizes and over-representation of severe cases, the incubation period for which may differ from that of mild cases. Evidence suggests an incubation period of 5-6 days^{7, 10, 123-134} with a range of 1-14 days^{7, 8, 11, 31, 34, 51, 126, 128, 130, 131, 135, 136} from infection to symptoms surfacing. Further analysis of 2,555 Chinese community cases indicates a longer incubation period of 9 days.¹³⁷ Lauer et al estimate that most (97%) of those who develop symptoms do so within 11.5 days of infection (95% CI, 8.2-15.6), consequently only a limited number of cases will potentially develop symptoms out-with the 14 days of self-isolation that is required following contact with a confirmed case.¹²⁵

Conclusion:

- The incubation period for most individuals is reported as 5-6 days (range 1-14 days).
- Self-isolation for 7 days is recommended for individuals with symptoms consistent with COVID-19.

- Self-isolation for 14 days is recommended for contacts of symptomatic cases.

Infectious period

Assessment of the clinical and epidemiological characteristics of SARS-CoV-2 cases suggests that, similar to SARS-CoV, patients are not infectious until the onset of symptoms.¹²⁶ In most cases, individuals are usually considered infectious whilst they have respiratory symptoms; how infectious an individual is likely depends on the severity of their symptoms and stage of their illness. Initial data from Wuhan suggested a median time from symptom onset to clinical recovery for mild cases of approximately 2 weeks, and 3-6 weeks for severe or critical cases however this data is likely biased by the fact that the majority of cases included in the study were hospitalized therefore the proportion of milder community cases may be underestimated.¹²⁶

Less is known about the duration of infectivity. Reports that suggest possible infectivity in the asymptomatic period are based on limited evidence from (largely retrospective observations during contact tracing) and identification of viral RNA in clinical samples post symptom resolution.^{10, 58, 63, 108, 109, 135, 138, 139} This prolonged viral shedding may not represent transmissible infectious viral cells; there is limited evidence regarding this. A report from a long term care facility in which two rounds of 'point prevalence' COVID-19 screening were carried out (1 week apart), found that more than half the residents (27 of 48) who had positive tests were asymptomatic at testing.¹⁴⁰ Further, 17 of 24 specimens (71%) from pre-symptomatic persons (those who were asymptomatic at testing but went on to develop disease) had viable virus by culture 1 to 6 days before the development of symptoms. Possible transmission events from these individuals were not reported. Identification of RT-PCR positivity in the incubation period has also been reported in South Korea; 41 out of 213 tested (19.2%) were asymptomatic at testing.¹⁴¹ Progression to disease was not reported; all individuals were isolated therefore transmission events in this cohort were not assessed. Initial analysis of the threshold cycle values ('Ct' value, which is inversely proportional to the viral load) of a small number of clinical samples revealed an approximately 200-fold higher viral load in symptomatic cases (compared to asymptomatic).¹¹⁷ However, a larger study found that the initial threshold cycle value of nasopharyngeal RNA in asymptomatic carriers was similar to that in pre-symptomatic and symptomatic patients.¹¹¹ The RNA negative-conversion of asymptomatic carriers occurred 15-20 days after admission, while the RNA negative-conversion for pre-symptomatic and

symptomatic patients occurred later, suggesting an earlier viral clearance for asymptomatic cases. From this, the authors deduced that the communicable period of asymptomatic cases (9.63 days) was shorter than pre-symptomatic patients (13.6 days). Analysis of 82 Chinese cases found that those with respiratory symptoms (cough) had a statistically significantly longer duration of positive testing by nasopharyngeal swab compared to patients presenting without respiratory symptoms (17 days vs. 13 days, $p = 0.041$).¹⁴²

Although transmission has been implicated in the pre-symptomatic/incubation period from contact tracing studies (as discussed previously) none of these reports had accompanying clinical data (i.e. RT-PCR testing in the incubation period). Therefore, the evidence for transmission from asymptomatic/pre-symptomatic cases is weak; further research is required. From limited international data, the balance of evidence is that, for mild cases of infection, infectivity (as determined by respiratory RT-PCR sampling) peaks at symptom onset and significantly reduces 7 days after the onset of symptoms but appears to take longer for severe cases.^{62, 126, 143-146} Wolfel et al assessed 9 cases in Munich, Germany and found that live virus could be isolated from respiratory samples taken within the first 7 days of symptoms but not from day 8 onwards, even though viral RNA could still be detected in samples.⁶² Live virus isolation may also be dependent on viral load; samples containing under 10^6 copies/mL (or copies per sample) never yielded an isolate.⁶² In the absence of histopathology, the same study analysed the presence of viral sgRNA which is only transcribed in infected cells and therefore can indicate the presence of actively-infected cells in samples. Throat swabs taken up to day 5 were positive while no sgRNA was detected thereafter. This single study suggests that as viral load reduces in the later stages of infection, so too does transmission risk. Wolfel et al estimate that, for patients beyond day 10 of symptoms and with less than 100,000 viral RNA copies per ml of sputum, early discharge with ensuing home isolation might be appropriate.⁶² Further research is required in the area of viral isolation to develop a robust evidence base. The infectious dose required for transmission has also not been determined.

Data from a number of studies has demonstrated a pattern with viral clearance with regards to clinical sample type; viral presence in respiratory samples appears to peak in the earlier stages of infection then decreases with time whilst the opposite has been observed with stool samples.^{58, 59, 61} Analysis of hospitalized cases in China indicated an association between hypertension and delayed viral clearance.^{144, 147} Hypertension is the most frequently reported CV comorbidity associated with COVID-19 infection; hypertensive

patients also have a higher mortality rate compared to normotensive patients.⁴¹ This has led to the suggestion that treatment with ACE2 inhibitors (antihypertensive medication) in patients with hypertension might facilitate SARS-CoV-2 to enter the targeted cells via ACE2 receptors in the respiratory system, and thus prolong the time of viral clearance.¹⁴⁴ Further research is required to detangle the association between severe disease, comorbidities, and delayed viral clearance.

Guidance from the ECDC recommends that COVID-19 patients may be discharged from hospital based on: a) clinical resolution of symptoms, and b) evidence for viral RNA clearance which would be 2 negative RT-PCR tests from respiratory specimens at 24 hrs interval at least 8 days after onset of symptoms, where testing capacity permits.¹⁴⁸ However in light of the widespread community transmission, clinical criteria should gain priority. This is consistent with Scottish and UK guidance which recommends discharge as soon as the patient is clinical well enough (i.e. symptoms may still be present).^{149, 150} Those discharged should self-isolate for 7 days (with absence of fever for 48 hours) and 14 days (with absence of fever for 48 hours) for patients who received critical care and/or are immunocompromised.^{149, 150}

Conclusion:

- Transmission is most likely to occur whilst an individual is symptomatic.
- In mild cases of infection, the risk of transmission is thought to significantly reduce after 7 days.
- In severe cases the risk of transmission may extend beyond 7 days therefore Transmission Based Precautions (TBPs) should remain in place for the duration of hospital admission or home isolation until cessation of symptoms.
- In hospital settings clinicians should consider extending isolation for some cases e.g. elderly, immunosuppressed if they remain symptomatic after 14 days until test results are available.
- Patients discharged from hospital should self-isolate for 7 days (14 days if critical care was received) with absence of fever for 48 hours.

2. Personal protective equipment

There was limited evidence for the assessment of the PPE requirements for the prevention of transmission of SARS-CoV-2. Determination of the PPE requirements for new pathogens is usually based on previous experience with similar pathogens and/or similarly-transmitted pathogens. Determination of the efficacy of PPE recommendations is based on retrospective analyses of possible transmission events to HCWs, where any associations with PPE worn at the time are assessed. Such assessments are considered to be low quality evidence and prone to confounding.

Surgical face masks

It is vital that a distinction is made between the evidence pertaining to fluid-resistant surgical face masks (FRSM) (Type IIR) and standard (non-fluid-resistant) surgical face masks (Type II). Surgical masks are tested against the safety standard BS EN 14683:2019; this series of tests measures the performance of a surgical mask in bacterial filtration efficiency (BFE), breathing resistance and splash resistance. Type II and Type IIR surgical masks are both tested against this standard with them needing to meet a minimum BFE of 98%; however only Type IIR masks must pass the splash resistance test with a resistance of at least 16.0kPa. The terms 'fluid resistant' and 'fluid repellent' are often used interchangeably to denote a Type IIR surgical mask, however, terminology may vary internationally and a 'fluid repellent' mask may occasionally describe a mask that does not meet the BS EN 14683:2019 splash resistance standard and which is not suitable for protection against splash or spray i.e. a Type II surgical mask. In the UK, when recommended for infection prevention and control purposes a 'surgical mask' will be a fluid-resistant (Type IIR) surgical mask.

Standard surgical face masks (i.e. Type II) can be worn by an infectious individual to prevent transmission.¹⁵¹⁻¹⁵³ To demonstrate this, a study by *Leung et al* tested the efficacy of surgical masks at reducing the detection of seasonal (non-COVID-19) coronavirus in exhaled breath from infected patients.¹⁵⁴ Coronavirus could be detected in ~40% of samples collected from non-mask wearers (n=10) but was not detected in exhaled air from patients that wore surgical masks (n=11). The masks used were Type II, i.e. they were not fluid-resistant. This study was limited by the small sample size – due in part to the fact that a large proportion of infected participants had undetectable viral shedding in exhaled

breath. Studies assessing Type II surgical masks have also reported reduced detection of seasonal influenza in exhaled breath in mask wearers.^{154, 155}

Whereas standard surgical face masks can be worn by an infectious individual to prevent transmission, it is the fluid-resistant nature of FRSM that provides additional protection to the wearer (e.g. HCW) against droplet-transmitted infectious agents. Guidance consistently recommends that HCWs should wear a Type IIR FRSM as PPE when caring for a patient known, or suspected, to be infected with an infectious agent spread by the droplet route.^{22, 151, 153, 156-160} In UK health and care settings, surgical masks must be fluid-resistant, 'CE' marked and compliant with Medical Device Directive (MDD/93/42/EEC) and the Personal Protective Equipment Regulations 2002.¹⁶¹⁻¹⁶⁶

Surgical masks do not provide protection against airborne particles and are not classified as respiratory protective devices.¹⁶⁷ Assessment of PPE use against similar coronaviruses i.e. severe acute respiratory virus (SARS), indicates that droplet precautions (i.e. surgical masks) are adequate. A case control study that compared PPE use in 241 non-infected HCWs and 13 infected HCWs with documented exposure to 11 index patients with SARS-CoV found that droplet precautions were adequate for prevention of nosocomial SARS where no aerosolisations are expected.¹⁶⁸ The non-infected staff who wore surgical masks and N95 respirators were significantly associated with non-infection but this was not the case for the non-infected staff that wore paper masks. Only 2 of the 13 infected HCWs wore respiratory protective equipment (RPE) (both paper masks). A systematic review and meta-analysis combining 6 case-control and 3 cohort studies, found that use of respirators/masks provided significant protection against SARS-CoV among exposed HCWs (OR=0.22; 95% CI: 0.12-0.40). Wearing surgical masks (OR=0.13; 95% CI: 0.03-0.62) or N95 respirators (OR=0.12; 95% CI: 0.06-0.26) (versus no RPE) both reduced the risk of SARS-CoV by approximately 80%. No protective effect was reported for disposable cotton or paper masks. The existing evidence base in the review was sparse and indications (and compliance) for mask/respirator use varied between the included studies.¹⁶⁹ Inadequate reporting of RPE/mask indications and compliance was a major limitation in a recent systematic review and meta-analysis conducted by *Bartoszek et al*, which included 4 RCTs and reported that, compared to N95 respirators, the use of medical masks was not associated with an increase in laboratory-confirmed viral respiratory infection or respiratory illness.¹⁷⁰ There was significant variation in surgical mask type between the included studies (Type IIR FRSMs were not used in every study). A recent update to a Cochrane systematic review that assessed full body PPE for the

prevention of exposure to highly infectious diseases (including COVID-19) found that covering more parts of the body leads to better protection but usually comes at the cost of more difficult donning or doffing and less user comfort, and may therefore even lead to more contamination.¹⁷¹ Certainty of the evidence was judged as low due to the fact that almost all findings were based on one or at most two small simulation studies.

For all non-AGP scenarios, there is no evidence that respirators offer any additional protection against droplet-spread infectious disease, including coronaviruses.

Conclusion:

- Health and care workers should wear a Type IIR fluid-resistant surgical face mask during any activities/procedures where there is a risk of blood, body fluids, secretions or excretions splashing or spraying onto their nose or mouth and when caring for a patient known or suspected to be infected with an infectious agent spread by the droplet route i.e. COVID-19.
- Symptomatic patients may wear either Type II or IIR fluid-resistant surgical masks if they can be tolerated.

Respiratory protective equipment (RPE)

The WHO defines an AGP as a medical or care procedure that creates the potential for airborne transmission of infections that may otherwise only be transmissible by the droplet route.²² It should also be recognised that as well as producing aerosols, these procedures produce larger droplet particles.²³⁻²⁵ During AGPs there is an increased risk of aerosol spread of infectious agents irrespective of the mode of transmission (contact, droplet, or airborne) and airborne precautions (FFP3 respirator and facial protection) must be implemented.¹⁷²

It is important to note that not all FFP3 respirators are fluid-resistant; valved respirators can be shrouded or unshrouded. Respirators with unshrouded valves are not considered to be fluid-resistant and therefore should be worn with a full face shield if blood or body fluid splashing is anticipated. This must be taken into consideration where FFP3 respirators are being used for protection against COVID-19 transmission.

Conclusion:

- Airborne precautions (FFP3 respirators) are required when providing care in high risk units ('AGP hotspots') and when performing AGPs on patients with suspected/confirmed COVID-19.

UK PPE guidance

For general patient care (i.e. non-AGP situations), the first edition of the UK IPC pandemic COVID-19 guidance initially recommended Type IIR FRSMs, disposable aprons and disposable gloves.¹⁴ The decision to wear eye protection was based on risk assessment (but considered essential when carrying out AGPs). Fluid-resistant long sleeve gowns were recommended for management of confirmed cases and when carrying out AGPs.¹⁴ FFP3 respirators were recommended when carrying out AGPs and when in high risk areas where AGPs are being conducted. The FFP3 recommendation was based on expert opinion from NERVTAG which recommended that airborne precautions should be implemented at all times in clinical areas considered AGP 'hot spots' e.g. Intensive Care Units (ICU), Intensive Therapy Units (ITU) or High Dependency Units (HDU) that are managing COVID-19 patients (unless patients are isolated in a negative pressure isolation room/or single room, where only staff entering the room need wear a FFP3 respirator).

The UK IPC pandemic COVID-19 guidance was updated on 2nd April 2020 with a move to PPE based on risk of exposure to possible (not suspected/confirmed) cases, with recommended ensembles for specific care areas/clinical situations.¹⁷³ The guidance states that *'incidence of COVID-19 varies across the UK and risk is not uniform and so elements of the updated guidance are intended for interpretation and application dependent on local assessment of risk'*. While this is not in line with the evidence base to date for COVID-19 as presented in this rapid review, it is based on the potential challenges in establishing whether patients and individuals meet the case definition for COVID-19 prior to a face-to-face assessment or care episode.

Specifically, FRSMs are recommended for direct patient care (within 2 metres) in inpatient, radiology, maternity and labour wards (2nd/3rd stage labour vaginal delivery – no AGPs), operating theatres (no AGPs), emergency departments/acute assessment areas, and when transferring possible (suspected) or confirmed cases.¹⁷³ Either a disposable plastic apron or a fluid-resistant gown can be worn, with the exception being when performing AGPs outside high risk acute care areas, when a gown must be worn. Eye protection

(single or reusable full face visor or goggles) is recommended at all times with the exception of inpatient care to any individuals in the extremely vulnerable group undergoing shielding.¹⁷³

AGP 'hot-spots', and consequently the locations requiring HCWs to don FFP3 respirators, were expanded to include ED resuscitation areas, wards with non-invasive ventilation, operating theatres, endoscopy units for upper respiratory/ENT or upper GI endoscopy, and any other clinical areas where AGPs are regularly performed.¹⁷³

There was also a move towards sessional use of PPE considering the recognised global shortage of PPE stockpiles and perhaps in recognition of the fact that the change in UK PPE recommendations are likely to result in greater use of PPE by a wider staff group which will deplete existing UK stocks.

On April 17th 2020, an additional section was added to the UK IPC pandemic COVID-19 guidance, '*Considerations for acute personal protective equipment (PPE) shortages*' which recommends (in addition to sessional use) reuse of FFP3/FF2/N95 respirators, fluid-resistant gowns or coveralls, goggles and face visors. PPE items which are to remain single-use (and non-sessional) are disposable gloves and aprons.

The safety and efficacy of extended use or re-use of PPE has not been extensively studied. An evidence summary by ECRI (Emergency Care Research Institute), a US company that evaluates medical devices, evaluated 21 laboratory studies and concluded that extended use (i.e. sessional use) of N95 respirators was preferable to reuse.¹⁷⁴ Mechanical failure (e.g. broken straps and poor sealing between the mask and the user's face) following only a few reuses was common across a number of FDA-cleared N95 respirators. The reported pathogen transfer risk from contact during donning and doffing during reuse was considered to be higher than the risk from sessional wear. Use of surgical masks or similar disposable covers over N95s during sessional wear were unlikely to result in significant adverse effects. Reuse would require disinfection however loss of filter performance was reported with some common disinfection methods. The methods for disinfection included humid heat, chemical disinfection, and ultraviolet germicidal irradiation (UVGI). The ECRI report summarises the findings from a number of decontamination studies conducted; steam sterilisation required 10 minutes at a minimum of 121°C to be effective however it may damage polymer fibres in the filter and compromise performance; chemical disinfection was limited by the risk of toxicity and chemical incompatibility with filter materials; UVGI penetration may be incomplete in multi-

layered N95 filters. UVGI is capable of inactivating coronaviruses including MERS-CoV and SARS-CoV however these tests were not conducted on any type of PPE.¹⁷⁵ UV radiation degrades polymers which presents the possibility that UVGI exposure may reduce the efficacy of respirators.¹⁷⁶ A previous study demonstrated degradation of 4 different types of N95 respirators at doses of 120-950 J/cm².¹⁷⁷ Attempts at using steam sterilisation of FFP respirators has shown promise however rigorous testing in line with EN standards for respirator efficacy is required.¹⁷⁸ None of the eight different decontamination methods tested on different N95 respirator models were suitable, failing in terms of ability to penetrate the filters and/or as a result of damage to the respirators.¹⁷⁹ The methods included UVGI, ethylene oxide, hydrogen peroxide gas plasma, hydrogen peroxide vapour, microwave-oven-generated steam, bleach, liquid hydrogen peroxide, and moist heat incubation (pasteurization). One study found disinfection using aerosolised peracetic acid and hydrogen peroxide to be effective at reducing contamination of a surrogate coronavirus bacteriophage on N95 respirators however the safety of these chemicals was not tested.¹⁸⁰

The extant UK IPC pandemic COVID-19 guidance does not recommend decontamination of respirators.¹⁷³ Respirators should be discarded if they become moist, visibly soiled, damaged, or become hard to breathe through. The ECDC recommends that, where reuse of respirators is considered as a last resort option to economise on use of PPE, the risk of the surface of the respirator becoming contaminated by respiratory droplets is considered to be lower when it is covered with a visor.¹⁸¹ However this ensemble is dependent on a plentiful supply of visors.

As highlighted in the ECRI report, the reported pathogen transfer risk from contact during donning and doffing during reuse was considered to be higher than the risk from sessional wear.¹⁷⁴ Unfortunately there is no evidence available to assess the impact on filtration efficacy or the risk of transmission associated with reuse of RPE in clinical settings. A study that assessed efficacy of Type IIR FRSMs and N95 respirators that were worn sessionally and reused did not include a reliable control group for comparison which prevented assessment of the efficacy of continuous wear/reuse.¹⁸² RPE was reported to be stored between shifts in a paper bag in lockers; the extent of reuse was not reported. Compared with continuous use of FRSMs, respirators were associated with more problems for the wearer including significantly greater discomfort, trouble communicating with the patient, headaches, difficulty breathing, and pressure on the nose.¹⁸² The WHO '*Rational use of PPE for COVID-19*' mentions that respirators can and have previously

been used for extended periods of time to treat multiple patients with the same diagnosis.¹⁸³ Whilst WHO state that there is evidence to support respirators maintaining their protection over longer periods of time, it may not be comfortable to use one respirator for longer than 4 hours and this should be avoided¹⁸³ as reuse may increase the potential for contamination and contact transmission of infectious agents (not just SARS-CoV-2). This risk must be balanced against the need to provide respiratory protection for HCWs providing care and to those performing AGPs. To reduce the risk of transmission associated with PPE reuse it is essential that health and care workers demonstrate stringent compliance with all other infection control precautions, hand hygiene, and environmental decontamination. Irrespective of the measure implemented, health care workers must have IPC education and training on the correct use of PPE and other IPC precautions, including demonstration of competency in appropriate procedures for donning and doffing PPE and hand hygiene. These issues are for consideration by the Health and Safety Executive (HSE). The HSE approved the sessional and reuse of PPE in the UK for COVID-19 and expects NHS Boards to have an agreed action plan that includes consideration of all measures to manage usage effectively.

Conclusion:

- Single use eye protection and single use RPE should be worn when performing AGPs.
- Sessional use of respirators is preferred over reuse.
- The decision to reuse PPE (respirators, fluid-resistant gowns or coveralls, goggles and face visors) should be based on a risk assessment considering the care activities, patient population, and the state of the PPE in question.

3. Hand hygiene

Most articles identified recommend that hand hygiene should be performed, however many do not specify the product(s) to be used in preventing the transmission of SARS-CoV-2. A number of guidance documents provide specific recommendations which differ only slightly.^{8, 12, 16} WHO and Public Health England support the use of soap and water, and alcohol-based hand rub (ABHR) when soap and water is not available and when hands are not visibly soiled.^{12, 16} Experimental evidence has shown that commercially-available ABHRS and WHO ABHR formulations are effective at inactivating

SARS-CoV-2 within a contact time of 30 seconds.¹⁸⁴ Commercially-available ABHRs have also shown efficacy against other coronaviruses included SARS-CoV and MERS-CoV.^{184,}

185

Conclusion:

- Hand hygiene should be performed with soap and water or, when hands are not visibly soiled, with ABHR.

4. Survival in the environment

A number of environmental sampling studies of isolation rooms occupied by COVID-19 patients and surrounding areas sampled various locations prior to environmental cleaning; virus was found on multiple room surfaces including the bed rail, locker, chair, light switches, sink, taps, floor, window ledge, PPE storage area, hand sanitizer dispensers, air outlet fan, elevator buttons, as well as the toilet bowl surface and door handle.^{19, 186-188} Personal items such as mobile phones, TV remotes, and medical equipment were also contaminated.^{19, 188} Viral samples were shown not to be viable, in the one study that assessed this.¹⁹ These studies highlight the potential for environmental contamination, particularly of frequently-touched areas. In light of limited data for SARS-CoV-2 regarding survival time in the environment, evidence was assessed from studies conducted with previous human coronaviruses including MERS-CoV and SARS-CoV. From largely experimental studies, human coronaviruses are capable of surviving on inanimate objects and can remain viable for up to 5 days at temperatures of 22-25°C and relative humidity of 40-50% (which is typical of air conditioned indoor environments).^{11, 53, 189-192} Survival is also dependent on the surface type.¹⁸⁹ An experimental study using a SARS-CoV-2 strain reported viability on plastic for up to 72 hours, for 48 hours on stainless steel and up to 8 hours on copper.¹⁹³ Viability was quantified by end-point titration on Vero E6 cells. A 99.9% viral titre reduction was observed after 2-3 days in waste water in an experimental study using human coronavirus 229E, suggesting low survivability in waste water.¹⁹⁴ Samples taken from the treated sewage outlet of a COVID-19 Chinese hospital were negative.¹⁹⁵ There is no current evidence that human coronaviruses are transmitted through contaminated drinking water.¹⁹⁶

Conclusion:

- Due to the uncertainty regarding the environmental survivability of SARS-CoV-2 in real-life conditions, it is essential that the environment is clutter free and frequency of routine cleaning is increased, particularly frequently-touched surfaces.

5. Environmental decontamination

Evidence for cleaning of the care environment for COVID-19 is limited; studies that evaluate the susceptibility of coronaviruses to cleaning/disinfectant products differ by their methodology and often use animal coronaviruses in experimental conditions.^{53, 185, 189} An experimental study using a SARS-CoV isolate, tested three different surface disinfectants but all required over 30 minutes exposure time to inactivate the virus to levels below detection.¹⁸⁵ Limited evidence suggests that coronaviruses are susceptible to chlorine-based disinfectants and ethanol-based antiseptics.^{189, 197} Kampf et al summarised the efficacy of various disinfectants against both human and animal coronaviruses and found that a concentration of 0.1% sodium hypochlorite was effective in 1 minute and, for the disinfection of small surfaces, 62-71% ethanol revealed a similar efficacy.¹⁸⁹ The WHO recommends that, for coronaviruses, commonly used hospital-level disinfectants such as sodium hypochlorite (at a concentration of 0.5%) are effective for cleaning environmental surfaces, and 70% ethanol is suitable for disinfecting small surfaces.¹⁶ A sampling study found that twice daily cleaning of frequently-touched areas using 5000 ppm of sodium dichloroisocyanurate (a source of free chlorine) resulted in negative swab results for COVID-19 in isolation rooms that had just been cleaned; samples taken from rooms prior to cleaning had multiple positive samples from frequently-touched areas.¹⁸⁶ Similar results were reported at a Chinese hospital in which surfaces were routinely wiped with 1000 mg/L chlorine-containing disinfectant every 4 hours in isolation ICUs and every 8 hours in general isolation wards; none of the environmental samples in these areas tested positive for SARS-CoV-2 contamination.¹⁹⁵

For situations where health and care settings are at capacity and/or have no breaks in admissions or bed occupancy, the opportunity to conduct a terminal clean or a deep clean may be limited. Solutions to this may include modification to the deep clean regime to allow as high a level of decontamination to be carried out during constant occupancy as possible.

In light of the concern raised regarding aerosol transmission following the identification of positive (but not viable) air samples from hospital rooms,^{18, 19, 186, 187} alternative decontamination techniques that offer air decontamination should be explored. Air disinfection using ultraviolet light, termed ultraviolet germicidal irradiation (UVGI) is accomplished via several methods: irradiating the upper-room air only, irradiating the full room (when the room is not occupied or protective clothing is worn), and irradiating air as it passes through enclosed air-circulation and heating, ventilation, and air-conditioning (HVAC) systems.¹⁹⁸ UVGI is also used in self-contained room air disinfection units. The room/area must be vacated during UVGI decontamination, which might be a problem in health and care settings experiencing constant occupancy, and/or full capacity and thus might be a barrier to the use of UVGI for routine decontamination. However, UVGI may be suitable for routine decontamination of care homes, where communal areas such as dining rooms/activity areas are vacated daily. A study conducted in an American nursing home found that use of a portable UVGI disinfection device for terminal cleaning of resident rooms, and weekly UVGI disinfection of shared areas (dining rooms and activity areas), was significantly associated with reduced respiratory infection rates ($p=0.017$) and hospitalisation by pneumonia ($p=0.006$).¹⁹⁹ There is the possibility that the manual cleaning (using a combined sodium hypochlorite-detergent cleaning agent) that preceded UVGI disinfection may have also influenced the observed infection rate reductions. Whole-room UVGI is capable of inactivating coronaviruses including MERS-CoV and SARS-CoV.¹⁷⁵ A review of UV decontamination technology by HPS recommended that UV light systems can be used as an additional measure when performing terminal room decontamination²⁰⁰ and this technology is already used in some health and care settings in the UK. Terminal decontamination is essential for reducing the risk of nosocomial transmission to the next room occupant, and will be particularly important as health and care settings begin to re-open.

Research conducted with NHS England Trusts to inform the Scientific Advisory Group for Emergencies (SAGE) suggests that nosocomial transmission of COVID-19 is occurring, with 8.2% of cases being diagnosed 14 days post-admission (inter-quartile range 3.8% to 12.0%). The survey demonstrated variation between Trusts in implementation of the latest IPC guidelines, and poor IPC practice in a number of areas. Concern was voiced regarding the lack of concise and comprehensive cleaning guidelines for COVID-19. Cleaning will be particularly important as outpatient/elective areas begin to re-open. There is an urgent need to address this in UK IPC pandemic COVID-19 guidance.

Conclusion:

- A combined detergent/disinfectant solution at a dilution of 1,000 parts per million available chlorine (ppm available chlorine (av.cl.)) should be used for transmission-based environmental cleaning.¹⁷² Small surfaces, and those which cannot be cleaned by chlorine-based agents, can be disinfected with 70% ethanol.
- Environmental decontamination must be carried out and frequency of environmental decontamination in COVID-19 care homes increased.
- Where terminal cleaning cannot be carried out due to constant occupancy, a modified enhanced clean should be carried out where possible.
- The use of UVGI should be considered where possible as part of both routine and terminal cleaning.

6. Areas for further research

An overarching limitation of all identified evidence is the novel nature of SARS-CoV-2 and the limited ability for robust research at the early stages of an outbreak.

More work is needed to improve and develop culture techniques to allow determination of the viability of viral particles detected in clinical and environmental samples. This will assist with determination of the infectious dose and will provide insight into the duration of infectivity, particularly in relation to the prolonged viral shedding that is observed in faecal samples.

Further research is required to determine the extent of atypical presentations and pre-symptomatic transmission and the overall impact of these on transmission. A robust epidemiological evidence base will assist with the development of infection control measures that are targeted and evidence-based.

Assessment of the efficacy of UVGI and other novel decontamination technologies for environmental decontamination and for the decontamination of PPE would inform COVID-19 IPC guidance and provide reassurance for health and care workers.

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